Article

A NEW HEMOSTATIC AGENT—ANKAFERD BLOOD STOPPER: MANAGEMENT OF GASTROINTESTINAL BLEEDING IN AN INFANT AND OTHER EXPERIENCES IN CHILDREN

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Ankaferd blood stopper (ABS) is a standardized medicinal plant extract that stimulates the formation of an encapsulated protein network that provides focal points for erythrocyte aggregation. It has a therapeutic potential to be used for the management of external hemorrhage. Here, the authors report an infant bleeding from peptic ulcer was stopped successfully by gastroscopic application of ABS and other cases that used topical ABS for mucosal bleedings are also presented.

Keywords Ankaferd, children, hemorrhage, hemostatic

Ankaferd blood stopper (ABS) is a unique medicinal plant extract that has been approved in the management of external hemorrhage and dental surgery bleedings in Turkey. It consists of a standardized mixture of 5 plants: Thymus vulgaris, Glycyrrhiza glabra, Vitis vinifera, Alpinia officinarum, and Urtica dioica. Each of them has some effect on hematological and vascular parameters and cellular proliferation [1]. The basic mechanism is the formation of an encapsulated protein network that provides for focal points for erythrocyte aggregation without acting on coagulation factors and platelets. Exposure to ABS seems to provide a tissue oxygenation
as well as a physiological hemostatic process without affecting any individual clotting factor [1, 2]. Also, ABS has a remarkable antimicrobial activity against different bacteria. The antimicrobial activity of ABS was tested against 102 clinical isolates in a previous study [3]. The isolates included Acinetobacter baumannii, Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Enterobacter species, Stenotrophomonas maltophilia, methicillin-resistant Staphylococcus aureus, methicillin-resistant coagulase-negative Staphylococcus, vancomycin-susceptible Enterococcus, and vancomycin-resistant Enterococcus. The researchers have reported that ABS was active against all these isolates.

Recently, a few clinical studies and case reports have been reported showing the efficiency of ABS as a clinically usable hemostatic agent [4–7]. It is currently used as solution, spray, and tampon form. We herein report an infant whose bleeding from peptic ulcer was stopped with endoscopical usage of ABS and other cases with several hematological diseases in whom mucosal bleedings were ceased with topical ABS.

**PATIENTS AND METHODS**

A 1-year-old boy who was treated with the hemophagocytic lymphohistiocytosis (HLH)-2004 protocol (dexamethasone 10 mg/m²/day, cyclosporine 6 mg/kg/day, etoposide 150 mg/m² twice a week) for primary hemophagocytic syndrome for 6 days was bleeding and vomiting and his hemoglobin level decreased from 11 to 7 g/dL [8]. His platelet count was $34 \times 10^9$/L, INR (international normalized ratio) was 1.1, activated partial thromboplastin time (aPTT) was 20 seconds, and fibrinogen level was 243 mg/dL. Intravenous omeprazole (4 mg/kg/day) and sucralfate (4 g/day orally [PO]) was started and dexamethasone was stopped. Along with random platelet transfusion, upper gastrointestinal endoscopy was performed and an actively bleeding ulcer on the duodenal mucosa was demonstrated (Figure 1). After informed consent was obtained from both parents, approximately 1 mL ABS solution was squirited over the ulcer surface and in a very short period white-grey adherent clot was developed on it and bleeding ceased (Figure 2).

The patient’s disease was not in remission and after he became stable, dexamethasone treatment was restarted with omeprazole at a dose of 2 mg/kg/day. On follow-up he is in clinical and hematological remission and receiving maintenance therapy of HLH-2004 protocol, which comprise pulse dexamethasone treatment every second week with a dose of 10 mg/m²/day for 3 days and intravenous etoposide 150 mg/m² every second week and also cyclosporine 6 mg/kg daily PO.

Recently, we also treated mucosal hemorrhage of children with several hematological diseases with ABS (wet tampon and spray form) successfully. The diagnoses and bleeding sites are shown in Table 1. In patients with aplastic anemia and acute myeloid leukemia (AML), although acute
hemorrhages were stopped with ABS, platelet suspensions were also given later. However, patient with Evans syndrome and Glanzmann thrombasthenia, we did not use any additional hemostatic agent or platelet suspension. Also, although patient with factor X deficiency received fresh frozen plasma (FFP) before dental surgery, gingival bleeding occurred and with ABS hemorrhage stopped within a minute.

Acute mucosal toxicity, hepatotoxicity, and nephrotoxicity were monitored. Neither local adverse effect nor systemic toxicity was observed in our patients.

FIGURE 2 The endoscopically application of ABS completely controlled the bleeding.
TABLE 1 Characteristics of Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/sex</th>
<th>Diagnosis</th>
<th>Abnormal hematological tests</th>
<th>Bleeding site</th>
<th>ABS form</th>
</tr>
</thead>
<tbody>
<tr>
<td>MK</td>
<td>8/M</td>
<td>Aplastic anemia</td>
<td>Platelet: $1.0 \times 10^9$/L</td>
<td>Gingiva, epistaxis</td>
<td>Spray; tampon</td>
</tr>
<tr>
<td>BK</td>
<td>16/F</td>
<td>Evans syndrome</td>
<td>Platelet: $8.0 \times 10^9$/L</td>
<td>Gingiva</td>
<td>Spray</td>
</tr>
<tr>
<td>NFT</td>
<td>7/M</td>
<td>Factor X deficiency</td>
<td>PT: 106 s ($N = 12–14$) aPTT: 100 s ($N = 32–36$)</td>
<td>Gingiva (postoperative dental surgery)</td>
<td>Spray</td>
</tr>
<tr>
<td>MHÖ</td>
<td>7/M</td>
<td>ALL, mucositis</td>
<td>—</td>
<td>Oral mucosa</td>
<td>Spray</td>
</tr>
<tr>
<td>OH</td>
<td>6/M</td>
<td>Aplastic anemia</td>
<td>Platelet: $7.0 \times 10^9$/L</td>
<td>Epistaxis</td>
<td>Tampon</td>
</tr>
<tr>
<td>AA</td>
<td>9/F</td>
<td>Fanconi aplastic anemia</td>
<td>Platelet: $2.0 \times 10^9$/L</td>
<td>Epistaxis</td>
<td>Tampon</td>
</tr>
<tr>
<td>CG</td>
<td>6/F</td>
<td>AML M3</td>
<td>Platelet: $22.0 \times 10^9$/L</td>
<td>Epistaxis</td>
<td>Tampon</td>
</tr>
</tbody>
</table>

Note. ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia.

DISCUSSION

Ankaferd blood stopper might be effective both in patients with normal hemostatic parameters and in patients with deficient primary or secondary hemostatic parameters [1–6]. It has been shown that blood cells, particularly erythrocytes, were found to aggregate rapidly (<1 seconds) in the presence of ABS, thereby participating in protein network formation. Although in that in vitro study the levels of coagulation factors II, VII, VIII, IX, X, XI, and XIII have not been affected by ABS, plasma fibrinogen antigen levels and total protein, albumin, and globulin levels have decreased after the addition of ABS [1]. It was suggested that Ankaferd-induced network formation depended upon interaction between ABS and blood proteins, mainly fibrinogen, and indicated that ABS could affect both fibrinogen and other proteins via agglutination of these proteins. Nevertheless, Uçar Albayrak et al reported a case with afibrinogenemia whose hemorrhagic wound was treated with ABS and considered that fibrinogen is not a necessary component of protein network [4]. Recently, ultrastructural and morphological analysis of ABS-induced coagulum was illustrated under scanning electron microscopy. Although this protein network is enriched principally with erythrocytes, it also causes augmentation of the primary and secondary hemostatic systems without disturbing individual coagulation factors or platelets [9].
Bleeding can lead to significant morbidity and mortality in the clinical setting, especially in the hematology departments. In our case, peptic ulcer bleeding at the duodenum was coagulated by ABS solution given endoscopically. Additional application of Ankaferd or other hemostatic agents was not needed. Mucosal bleedings of our other patients with severe thrombocytopenia or hemorrhagic diathesis such as Glanzmann thrombasthenia and factor X deficiency were also stopped in a very short time with wet tampon or spray form.

There are a few previous studies concerning gastrointestinal endoscopic application of ABS [5, 7, 10, 11]. Our patient is the first case showing that ABS can be used endoscopically safely and effectively in children. Also either nasal or gingival mucosal hemorrhage due to thrombocytopenia/thrombasthenia or coagulopathy may potentially be treated with topical ABS effectively. Therefore we believe that this unique and promising agent has a great therapeutic potential to be used in the management of hemorrhage in the pediatric population. Controlled clinical studies should be performed concerning the efficiency of this promising medication both in normal and pathological hemostasis.

Declaration of Interest: The authors confirm that there is no conflict of interest.

REFERENCES